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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/455,486	12/06/1999	DANIEL E. AFAR	1703-011.US2	5189

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	33

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/455,486	AFAR ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

--The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

THE REPLY FILED 04 August 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *6* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *04 August 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☒ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See attachment*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1 and 44-48*.

   Claim(s) withdrawn from consideration: *4-18,20,21 and 24-43*.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☒ Other: *Attachment*

Gary B Nickol

Response to Arguments

The response filed August 4, 2003 (Paper No. 30) has been entered into the record.

As a first matter, Applicants argue (Paper No. 30, page 2) that the finality of the rejection (issued in Paper No. 27) is unjustified because the finality does not take account of the Declaration filed by Dr. Faris in response to the prior final rejection. This argument has been considered but is not found persuasive. The finality of the rejection issued in Paper No. 27 was issued solely in response to the new amendments filed together with the request for continued examination (RCE) in Paper No. 25, the latter of which did not mention the Faris Declaration. Furthermore, the Faris Declaration was previously considered in Paper No. 23 as so acknowledged by Applicants on page 3 of Paper No. 30. It is now that applicants wish to re-address said Declaration. Thus, the request to withdraw finality is denied.

Applicants have further submitted a declaration by Dr. Karen Morrison attesting that the use of STEAP-2 polypeptide for diagnostic purposes is disclosed throughout the specification and that the application provides various disclosures regarding the use of immunohistochemical techniques. In Item 6, page 2 of the Declaration, Dr. Morrison further points out that the application explicitly discloses the use of STEAP-2 as a diagnostic wherein one can evaluate the "levels" of STEAP-2 as an indication of whether that tissue is malignant. This argument has been considered but is not found persuasive. The issues addressing the predictability of the STEAP-2

polypeptide as a marker for cancer diagnosis have been previously considered throughout prosecution, beginning with Paper No.11, Item 2, pages 8-9. These arguments make it clear that the specification provides insufficient guidance and or objective evidence to one of skill in the art that the protein will predictably enable the diagnosis of cancer. Applicants further newly argue (page 4) that because expression of STEAP-2 is predominantly restricted to the prostate, any expression in other tissues which do not normally express STEAP-2 is evidence of metastasis (Morrison Declaration, Item 15, page 5). This argument has been considered but is speculative, at best. To the extent that applicants are suggesting that STEAP-2 is a marker for metastatic disease, the specification fails to provide a predictable nexus between the diagnosis or detection of metastatic disease with the expression of the STEAP-2 polypeptide in tissues that do not normally express STEAP-2. The specification provides neither guidance on nor exemplification of how to correlate STEP-2 protein expression with the ability to provide a diagnostic evaluation of an oncogenic disorder. Thus, in the absence of any correlation between the claimed encoded antigen with any known disease or disorder, any information obtained from various expression profiles in both normal and diseased tissue only serves as the basis for further research on the observation itself. Therefore, absent evidence of the protein's expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use the antigen in any diagnostic setting without undue experimentation.

The Morrison declaration also presents new arguments directed to the phenomenon of altered subcellular protein localization in a disease state (Item 10) which has been demonstrated with MUC1 and Her2 protein expression. These arguments have been considered but are not

found persuasive because the specification fails to teach any association between the altered subcellular localization of the *claimed* polypeptide in malignant tissue versus normal tissue.

Applicants have also issued a second declaration executed by Dr. Mary Faris (Paper No. 31) in which applicants argue (Paper No.30, page 4-5) that the specification as filed indicates that STEAP-2 functions as a calcium ion channel which itself provides a valuable screening tool for compounds that will exhibit anti-tumor functions. The Faris Declaration (Item 6, page 3) further argues that data shows that STEAP-2 functions in achieving drug resistance wherein the results indicated that expression of STEAP-2 imparts resistance to chemotherapeutic agents such as paclitaxel, and allows survival of prostate cancer cells. These arguments have been considered but are not found persuasive because the specification and claims as originally filed do not provide sufficient guidance as to the predictable and enabled use of the STEAP-2 polypeptide with regards to ion channels and or drug resistance with palcitaxel. Although the specification alludes to the possibility that the STEAP family is involved in ion channels, among other functions, there is nothing in the specification to suggest the specific use of STEAP-2 in concert as a screening tool with regards to calcium ion flux. There are a multitude of ion (i.e., hydrogen, sodium, potassium, chloride, etc.) channels that are highly regulated in many different types of cells, and the postulation that STEAP-2 may be generically involved with ion flux does not lend sufficient guidance or reasonable predictably to the use of the protein as a screening tool with regards to calcium ion transport. Furthermore, the specification fails to provide sufficient guidance with respect to the role of STEAP-2 in prostate cancer survival with regards to drug resistance. The specification does not teach nor lend support to any of the latter evidence. Furthermore, these finding were performed in-vitro in PC-3 cells. Those of skill in the art

recognize that in vitro assays and or cell-cultured based assays are generally useful to observe basic physiological and cellular phenomenon such as screening the effects of potential drugs. However, clinical correlations are generally lacking. The greatly increased complexity of the in vivo environment as compared to the very narrowly defined and controlled conditions of an in-vitro assay does not permit a single extrapolation of in vitro assays to human "diagnostic" efficacy with any reasonable degree of predictability. In vitro assays cannot easily assess cell-cell interactions that may be important in a particular pathological state. Furthermore it is well known in the art that cultured cells, over a period time, lose phenotypic characteristics associated with their normal counterpart cell type.

Thus, all of applicant's arguments have been carefully considered but are not found persuasive.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
September 25, 2003

Gary B Nickol